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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/579,025

10/19/2006

Dennis L. Panicali

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EXAMINER

SHEN, WU CHENG WINSTON

ART UNIT

PAPER NUMBER

1632

NOTIFICATION DATE

DELIVERY MODE

12/28/2009

ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No. 10/579,025	Applicant(s) PANICALI ET AL.	
	Examiner WU-CHENG Winston SHEN	Art Unit 1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 09/14/2009.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,7-10,12,13 and 16-22 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,7-10,12,13 and 16-22 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 11 May 2006 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date <u>11/19/2009</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Applicant's claim amendments filed on 09/14/2009 has been entered.

Claims 2-6, 11, 14, 15, and 23-44 are cancelled. Claims 1, 7, 8, 12, 13, 16, 17, and 21 are amended. Claims 1, 7-10, 12, 13, and 16-22 are pending.

Claims 1, 7-10, 12, 13, and 16-22 are currently under examination to the extent of the following elected species: an orthopox virus vector as recited in claim 7; MUC-1 as recited in claim 12; and MVA as recited in claim 20

This application 10/579,025 filed on 10/19/2006 is a 371 of PCT/US2004/038643 filed on 11/12/2004 which claims benefit of 60/519,354 filed on 11/12/2003.

Claim Objections

1. Previous objection of claims 1, 7-10, 12, 13, and 16-22 for recitation of claim limitation drawn to a non-elected invention, is ***withdrawn*** because the claims have been amended.

Amended claim 1 filed on 09/14/2009 reads as follows: A method for inducing an immunological response against a malignant pancreatic cell in an individual, said wherein the method comprises (a) selecting an individual having malignant pancreatic cells or at risk for developing such a pancreatic tumor, (b) administering to the individual a first poxvirus vector containing one or more DNA segments that encode (i) carcinoembryonic antigen (CEA) or an antigen portion thereof and (ii) mucin (MUC) or an antigen portion thereof or a modified version thereof, and (c) at regular intervals thereafter administering at least a second poxvirus vector containing a one or more DNA segments that encode (i) carcinoembrvonic antigen (CEA) or an antigen portion thereof and (ii) mucin (MUC) or an antigenic portion thereof or a modified version thereof, such that an immunological response against the malignant pancreatic cell is induced in the individual.

2. Claim 1 objected to because of the following informalities: Amended claim 1 filed on 09/14/2009 recites limitation “(c) at regular intervals thereafter administering at least a second poxvirus vector containing a one or more DNA segments” which should read “(c) at regular intervals thereafter administering at least a second poxvirus vector containing one or more DNA segments”. Appropriate correction is required.

Claim Rejection - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

3. Claims 1, 7-10, 12, 13, and 16-22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. *This rejection is necessitated by claim amendments filed on 09/14/2009.*

Amended claim 1 filed on 09/14/2009 reads as follows: A method for inducing an immunological response against a malignant pancreatic cell in an individual, said wherein the method comprises (a) selecting an individual having malignant pancreatic cells or at risk for developing such a pancreatic tumor, (b) administering to the individual a first poxvirus vector containing one or more DNA segments that encode (i) carcinoembryonic antigen (CEA) or an antigen portion thereof and (ii) mucin (MUC) or an antigen portion thereof or a modified version thereof, and (c) at regular intervals thereafter administering at least a second poxvirus vector containing a one or more DNA segments that encode (i) carcinoembrvonic antigen (CEA) or an antigen portion thereof and (ii) mucin (MUC) or an antigenic portion thereof or a modified

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version thereof, such that an immunological response against the malignant pancreatic cell is induced in the individual.

The limitation “or a modified version therefore” recited in (b) and (c) of claim 1 is unclear. It is noted that a gene can be modified to the extent of becoming a totally random sequences. In the absence of recitation of specific modifications, the metes and bounds “a modified version therefore” cannot be determined. Claims 7-10, 12, 13, and 16-22 depend from claim 1.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

4. Claims 1, 7-10, 12, 13, and 16-22 remain rejected under 35 U.S.C. 103(a) as being unpatentable over **Laidlaw et al.** (U.S. patent 7,273,605, issued date 09/25/2007, effective filing date 11/30/2001) in view of **Pecher** (WO 01/24832, PCT/DE00/03443, filed on 09/26/2000; this document is cited as reference AA in the IDS filed by Applicant on 07/09/2008), and **Kotera et al.** (Kotera et al., Humoral immunity against a tandem repeat epitope of human mucin MUC-1 in sera from breast, pancreatic, and colon cancer patients. *Cancer Res.* 54(11):2856-60, 1994). Applicant's arguments filed 09/14/2009 have been fully considered and they are not persuasive.

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Previous rejection is ***maintained*** for the reasons of record advanced on pages 5-11 of the office action mailed on 05/12/2009.

For the clarity and completeness of this office action, the rejection for the reasons of record advanced on pages 5-11 of the office action mailed on 05/12/2009, is reiterated below with revisions addressing claim amendments filed on 09/14/2009.

Amended claim 1 filed on 09/14/2009 reads as follows: A method for inducing an immunological response against a malignant pancreatic cell in an individual, said wherein the method comprises (a) selecting an individual having malignant pancreatic cells or at risk for developing such a pancreatic tumor, (b) administering to the individual a first poxvirus vector containing one or more DNA segments that encode (i) carcinoembryonic antigen (CEA) or an antigen portion thereof and (ii) mucin (MUC) or an antigen portion thereof or a modified version thereof, and (c) at regular intervals thereafter administering at least a second poxvirus vector containing a one or more DNA segments that encode (i) carcinoembryonic antigen (CEA) or an antigen portion thereof and (ii) mucin (MUC) or an antigenic portion thereof or a modified version thereof, such that an immunological response against the malignant pancreatic cell is induced in the individual.

Claims 6-10 and 17-21 further limit to specified orthopox vector and avipox vector for expression of carcinoembryonic antigen (CEA) and mucin (MUC). Claims 12, 13 and 16 further limit the recited mucin (MUC), various recited mucins (MUCs). Claim 22 further limits to recited set interval for administration.

Laidlaw et al. teaches a method which comprises administering a priming composition (which comprises a first non-replicating viral vector) and a boosting composition (which comprises a second non-replicating viral vector) to a subject to treat and/or prevent a cancer.

Laidlaw et al. teaches a viral particle comprising such a genome and its use to deliver a

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nucleotide of interest (NOI) to a target cell, and a fowlpox virus genome which has modifications in one or more wild-type FPV genes (See abstract, lines 5-10 of column 2, lines 57-60 of column 13, Laidlaw et al.).

With regard to the limitations pertaining to poxvirus, orthopox virus, avipox vector, and MVA recited in claims 7-10, and 17-21 of instant application, Laidlaw et al. teaches poxviruses have been exploited as recombinant vectors for the heterologous expression of foreign proteins. In particular, recombinant vaccinia virus has been studied as a tool for transient expression of genes in mammalian cells and an experimental recombinant vaccine vector (See lines 17-22, column 1, Laidlaw et al.). Laidlaw et al. teaches the family of poxviruses can be split into two subfamilies, the *Chordopoxvirinae* and the *Entomopoxvirinae*. The *Chordopoxvirinae* (poxviruses of vertebrates) include geni of orthopoxviruses and avipoxviruses. In a preferred embodiment the present invention provides a vaccine, priming or boosting composition which comprises a non-replicating pox virus vector. (See lines 41-50, column 6, Table 2, Laidlaw et al.). Laidlaw et al. teaches that concern about the capacity of vaccinia virus to replicate in mammalian cells has limited its clinical use and led to the search for safer alternatives, and these include attenuated vaccinia viruses, such as modified vaccinia Ankara (MVA) (See lines 38-41, column 1, Laidlaw et al.).

With regard to the limitation orthopox vector is administered before the avipox vector is administered recited in claim 21, Laidlaw et al. teaches that the two viral vectors maybe derived from viruses belonging to the same family (such as pox viruses) but different geni (e.g. the genus of orthopoxviruses and the genus of avipoxviruses) (See lines 40-47, column 7, Laidlaw et al.).

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With regard to the limitation the limitation the set interval is 20 days to 90 days, recited in claim 22, Laidlaw et al. teaches various prime-boost immunization regimes using different poxvirus vectors, such as 3-4 weeks intervals (See Example 14, columns 31-32, Laidlaw et al.).

With regard to carcinoembryonic antigen (CEA), mucin (MUC) as tumor associated antigens, Laidlaw et al. teaches nucleotide of interest (NOI) may, for example, be or encode one of the following: an antigen, cytokines, immune co-stimulatory molecules, immunomodulatory molecules. In one preferred embodiment, the NOI is capable of encoding a disease (e.g. cancer) associated antigen. Exposure to an antigen in the context of a fowlpox vector may provoke or boost immune responses to the antigen such that an existing or subsequent challenge is dealt with more effectively. (See lines 37-53, column 13, Laidlaw et al.). Laidlaw et al. teaches the target antigen may be an antigen which is recognized by the immune system after infection with the disease; and for cancers, preferred colon cancer antigens: CEA, MUC-1, MAGE-12, mutant P53 whereas preferred breast cancer antigens are MUC-1, HER2, CEA (See lines 19-30, column 20, Laidlaw et al.). Laidlaw et al. teaches number of other compositions may be employed in heterologous vaccination programs. If the genome/particle of the present invention comprises an NOI (optionally capable of encoding a POI, protein of interest), then preferably the other composition comprises the same NOI or POI. Other compositions, in addition to pox virus vectors, include "naked DNA", non-viral vector systems and other viral vector systems, and naked DNA (or RNA) may be linear or circular (for example, a plasmid). (See lines 48-57, column 14, Laidlaw et al.). Furthermore, related to immunization with two antigens, Laidlaw et al. teaches immunization of C57BL/6 mice using pSG2.ME1 and/or FP9.ME1 elicited IFN γ -secreting T cells against the LCMV epitopes (H-2^b), but not against the tumour epitopes (H-2^b)

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(FIGS. 17A-17B). The total frequency of IFN γ -secreting T cells elicited against LCMV epitopes by prime/boost immunization with pSG2.ME1/FP9.ME1 was significantly higher than that elicited by homologous immunisation with FP9.ME1 (P w 0.003) alone or pSG2.ME 1 (P=0.016) alone (See lines 60-67, column 46, Laidlaw et al.).

Laidlaw et al. does not explicitly teach a first and a second vector containing one or more DNA segments that encode (i) carcinoembryonic antigen (CEA) or an antigen portion thereof and (ii) mucin (MUC) or an antigen portion thereof for inducing immunological response against a malignant pancreatic cell.

Pecher teaches a pharmaceutical composition for treating and preventing human tumors, which express the tumor antigen carcinoembryonic antigen (CEA) and/or the tumor antigen mucin, and to the use thereof as a vaccine in humans for activating the immune system. The pharmaceutical composition is provided comprising a plasmid which contains the gene for the human carcinoembryonic antigen (CEA) SEQ No. 2., and another plasmid which contains the human mucin gene MUC1, active fragments thereof or at least 3 repeats of amino acid sequence SEQ No. 1, which reads on wobble MUC-1 or wobbled mini-MUC recited in claim 16 of instant application (See abstract, Pecher, W/O 01/24832, 2000). It is noted that Laidlaw et al. teaches that a number of other compositions may be employed in heterologous vaccination programs. If the genome/particle of the present invention comprises an NOI (optionally capable of encoding a POI), then preferably the other composition comprises the same NOI or POI. Other compositions include "naked DNA", non-viral vector systems and other viral vector systems (See lines 48-54, column 14, Laidlaw et al.).

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Kotera et al. teaches humoral immunity against a tandem repeat epitope of human mucin MUC-1 in sera from breast, pancreatic, and colon cancer patients.

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time of the invention to combine the teachings of Laidlaw et al. regarding a method which comprises administering a priming composition (which comprises a first non-replicating viral vector) and a boosting composition (which comprises a second non-replicating viral vector) to a subject to treat and/or prevent a cancer; a viral particle comprising such a genome and its use to deliver a nucleotide of interest (NOI) to a target cell, and a poxvirus vector or a plasmid for expression of NOI; and both CEA and MUC-1 being preferred colon cancer antigens as well as breast cancer antigens, with (i) the teachings of Pecher regarding the pharmaceutical composition is provided comprising a plasmid which expresses tumor antigen carcinoembryonic antigen (CEA) and/or the tumor antigen mucin, active fragments thereof, and (ii) the teachings of Kotera et al. regarding humoral immunity against a tandem repeat epitope of human mucin MUC-1 in sera from breast, pancreatic, and colon cancer patients, to arrive at the claimed methods for method for inducing an immunological response against a malignant pancreatic cell in an individual, comprising the recited steps.

One having ordinary skill in the art would have been motivated to combine the teachings of Laidlaw et al., Pecher, and Kotera et al. because (i) Pecher explicitly teaches a pharmaceutical composition for treating and preventing human tumors, which express the tumor antigen carcinoembryonic antigen (CEA) and the tumor antigen mucin, and to the use thereof as a vaccine in humans for activating the immune system against breast and colon cancer cells, (ii) Laidlaw et al. teaches a poxvirus vector or a plasmid vector for the expression of CEA and

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MUC-1, which are established tumor associated antigens (TAAs) for colon and breast cancers, and (iii) Kotera et al. teaches humoral immunity against a tandem repeat epitope of human mucin MUC-1 in sera from pancreatic, colon, and breast cancer patients.

There would have been a reasonable expectation of success given (i) successful establishment of various prime-boost immunization regimes for clinical trials using combination of poxvirus vectors each expresses a NOI, which encodes a polypeptide or an antigenic determinant that induces immunological response in an individual, and CEA and MUC-1 are preferred tumor associated antigens for immunization against breast and colon cancer cells, by the teachings of Laidlaw et al., (ii) a pharmaceutical composition for treating and preventing human tumors, which express the tumor antigen carcinoembryonic antigen (CEA) and express the tumor antigen mucin, and to the use thereof as a vaccine in humans for activating the immune system, and the pharmaceutical composition comprising a plasmid expressing the tumor antigen carcinoembryonic antigen (CEA, SEQ ID No:2) and the tumor antigen mucin (MUC1), by the teachings of Pecher, and (iii) humoral immunity against a tandem repeat epitope of human mucin MUC-1 in sera from breast, pancreatic, and colon cancer patients, by the teachings of Kotera et al.

Thus, the claimed invention as a whole was clearly *prima facie* obvious.

Applicant's arguments

Applicant argues that for subject matter defined by a claim to be considered obvious, the Office must demonstrate that the differences between the claimed subject matter and the prior art "are such that the subject matter as a whole would have been obvious at the time the invention

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was made to a person having ordinary skill in the art to which said subject matter pertains." 35 U.S.C. § 103(a); see also *Graham v. John Deere Co.*, 383 U.S. 1, 148 U.S.P.Q. 459 (1966). The ultimate determination of whether an invention is or is not obvious is based on certain factual inquiries including: (1) the scope and content of the prior art, (2) the level of ordinary skill in the prior art, (3) the differences between the claimed invention and the prior art, and (4) objective evidence of nonobviousness. *Graham*, 383 U.S. at 17-18, 148 U.S.P.Q. at 467. Applicant argues that consideration of the aforementioned *Graham* factors here indicates that the present invention, as defined by the pending claims, is unobvious in view of the cited references (See page 6 of Applicant's remarks filed on 09/14/2009).

Applicant argues that none of the cited references discloses a prime-boost protocol, wherein administration of a first poxvirus vector comprising two tumor-associated antigens (CEA and MUC) is followed by subsequent administrations of a second poxvirus vector comprising two tumor-associated antigens (CEA and MUC) for the induction of an immune response against malignant pancreatic cancer cells, as required by the pending claims. The Laidlaw reference merely discloses the administration of a first viral vector comprising one or more epitopes of a single target antigen and a second viral vector comprising one or more epitopes of the same target antigen. The Laidlaw reference discloses that the target antigen can be a tumor antigen, such as a breast, colon, or cervical cancer antigen, which includes CEA and MUC-1, but does not disclose the administration of the two different antigens (i.e., CEA and MUC-1) in each of the first and second vectors (See pages 7-8 of Applicant's remarks filed on 09/14/2009).

Applicant argues that the Pecher and Kotera references do not remedy the deficiencies of

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the Laidlaw reference. The Abstract of the Pecher reference (the other portions of the Pecher reference are not translated into English) discloses a pharmaceutical composition comprising a plasmid (naked DNA) comprising the gene encoding MUC-1 and/or another plasmid (naked DNA) comprising the gene encoding CEA for preventing or treating human tumors. Thus, CEA and MUC are not in the same vector, let alone in a viral vector, such as a poxvirus vector, as required by the pending claims. The Kotera reference merely discloses the presence of antibodies against a tandem repeat epitope of MUC-1 in sera from breast, pancreatic, and colon cancer patients. Applicant states that the specification describes a Phase I clinical trial, which established the preliminary safety and efficacy profiles of targeted cancer immunotherapy using a prime-boost protocol in patients with advanced pancreatic cancer (see paragraphs 235-236 and 244-251). Applicant states that as confirmed by the post-filing Kaufman reference (Journal of Translational Medicine, 5:60 (2007); a copy of which is submitted herewith), a prime-boost protocol comprising administration of a first poxvirus vector comprising the tumor-associated antigens CEA and MUC followed by subsequent administrations of a second poxvirus vector comprising CEA and MUC, as recited in the pending claims, resulted in the development of a significant increase in antigen- specific (CEA or MUC) immune response in patients (see, e.g., page 6, column 2) (See page 8 of Applicant's remarks filed on 09/14/2009).

Response to Applicant's arguments

Applicant is reminded that the claimed method as a whole was clearly *prima facie* obvious based on the collective teachings of Laidlaw et al., Pecher, and Kotera et al., not based on individual reference viewed separately. The claimed method as a whole was clearly *prima*

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facie obvious because (i) Pecher explicitly teaches a pharmaceutical composition for treating and preventing human tumors, which express the tumor antigen carcinoembryonic antigen (CEA) and the tumor antigen mucin, and to the use thereof as a vaccine in humans for activating the immune system, (ii) Laidlaw et al. teaches a poxvirus vector or a plasmid vector for the expression of CEA and MUC-1, which are established tumor associated antigens (TAAs) for colon and breast cancers, and (iii) Kotera et al. teaches humoral immunity against a tandem repeat epitope of human mucin MUC-1 in sera from pancreatic, colon, and breast cancer patients.

It is noted that the teachings by Pecher regarding “a pharmaceutical composition for treating and preventing human tumors, which express the tumor antigen carcinoembryonic antigen (CEA) and/or the tumor antigen mucin, and to the use thereof as a vaccine in humans for activating the immune system” certainly reads on “a pharmaceutical composition for treating and preventing human tumors, which express the tumor antigen carcinoembryonic antigen (CEA) and the tumor antigen mucin, and to the use thereof as a vaccine in humans for activating the immune system”. Furthermore, related to immunization with two antigens, Laidlaw et al. teaches immunization of C57BL/6 mice using pSG2.ME1 and/or FP9.ME1 elicited IFN γ -secreting T cells against the LCMV epitopes (H-2^b), but not against the tumour epitopes (H-2^b) (FIGS. 17A-17B). The total frequency of IFN γ -secreting T cells elicited against LCMV epitopes by prime/boost immunization with pSG2.ME1/FP9.ME1 was significantly higher than that elicited by homologous immunization with FP9.ME1 (P w 0.003) alone or pSG2.ME 1 (P=0.016) alone (See lines 60-67, column 46, Laidlaw et al.).

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With regard to the arguments regarding expression of CEA and MUC genes from a poxvirus vector is non-obvious by the cited references, the arguments have been fully considered and found not persuasive. It is noted that Laidlaw et al. specifically teaches that a number of other compositions may be employed in heterologous vaccination programs. If the genome/particle comprises an NOI (optionally capable of encoding a POI), then preferably the other composition comprises the same NOI (nucleotides of interest) or POI (proteins of interest). Other compositions include "naked DNA", non-viral vector systems and other viral vector systems (See lines 48-54, column 14, Laidlaw et al.). Using either plasmid or viral vector to express CEA and MUC is certainly obvious based on the combined teachings of Laidlaw et al. and Pecher.

It is noted that Applicant's provision of post-filing art by Kaufman et al. (*Journal of Translational Medicine*, 5: 60 (2007) provides evidence that the claimed methods are enabled. However, Kaufman et al. does not provide any evidence that the claimed methods are not *prima facie* obvious by the collective teachings of Laidlaw et al., Pecher, and Kotera et al.

Conclusion

5. No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO

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MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Any inquiry concerning this communication from the examiner should be directed to Wu-Cheng Winston Shen whose telephone number is (571) 272-3157 and Fax number is 571-273-3157. The examiner can normally be reached on Monday through Friday from 8:00 AM to 4:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the supervisory patent examiner, Peter Paras, Jr. can be reached on (571) 272-4517. The fax number for TC 1600 is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private

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/Wu-Cheng Winston Shen/

Patent Examiner

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